SmithKline Beecham—Cont.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate carcinogenic potential of mupirocin calcium have not been conducted.

Results of the following studies performed with mupirocin calcium or mupirocin sodium *in vitro* and *in vivo* did not indicate a potential for mutagenicity: rat primary hepatocyte unscheduled DNA synthesis, sediment analysis for DNA strand breaks, *Salmonella* reversion test (Ames), *Escherichia coli* mutation assay, metaphase analysis of human lymphocytes, mouse lymphoma assay, and bone marrow micronuclei assay in mice.

Reproduction studies were performed in rats with mupirocin administered subcutaneously at doses up to **40** times the human intranasal dose (approximately 20 mg mupirocin per day) on a mg/m^2 basis and revealed no evidence of impaired fertility from mupirocin sodium.

Pregnancy

Teratogenic Effects. Pregnancy Category B. Reproduction studies have been performed in rats and rabbits with mupirocin administered subcutaneously at doses up to 65 and 130 times, respectively, the human intranasal dose (approximately 20 mg mupirocin per day) on a mg/m^2 basis and revealed no evidence of harm to the fetus due to mupirocin. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when *Bactroban* Nasal is administered to a nursing woman.

Pediatric Use

Safety in children under the age of 12 years has not been established. (See CLINICAL PHARMACOLOGY.)

ADVERSE REACTIONS

Clinical Trials

In clinical trials, 210 domestic and 2,130 foreign adult subjects/patients received *Bactroban* Nasal ointment. Less than 1% of domestic or foreign subjects and patients in clinical trials were withdrawn due to adverse events.

The most frequently reported adverse events in foreign clinical trials were as follows: rhinitis (1.0%), taste perversion (0.8%), pharyngitis (0.5%).

In domestic clinical trials, 17% (36/210) of adults treated with *Bactroban* Nasal ointment reported adverse events thought to be at least possibly drug-related. The incidence of adverse events thought to be at least possibly drug-related that were reported in at least 1% of adults enrolled in domestic clinical trials were as follows:

ADVERSE EVENTS (≥ 1% INCIDENCE)-ADULTS IN U.S. TRIALS

	% of Subjects/Patients Experiencing Event *Bactroban* Nasal 2% (n=210)
Headache	9%
Rhinitis	6%
Respiratory disorder, including upper respiratory tract congestion	5%
Pharyngitis	4%
Taste perversion	3%
Burning/Stinging	2%
Cough	2%
Pruritus	1%

The following events thought possibly drug-related were reported in less than 1% of adults enrolled in domestic clinical trials: blepharitis, diarrhea, dry mouth, ear pain, epistaxis, nausea and rash.

All adequate and well-controlled clinical trials have been performed using *Bactroban* Nasal ointment, 2% in one arm and the vehicle ointment in the other arm of the study. No adequate and well-controlled safety data are available from direct, head-to-head comparative studies of this product and other products for this indication.

OVERDOSAGE

Following single or repeated intranasal applications of *Bactroban* Nasal to adults, no evidence for systemic absorption of mupirocin was obtained. Intravenous infusions of 252 mg, as well as single oral doses of 500 mg of mupirocin, have been well tolerated in healthy adult subjects. There is no information regarding local overdose of *Bactroban* Nasal or regarding oral ingestion of the nasal ointment formulation.

DOSAGE AND ADMINISTRATION

(See INDICATIONS AND USAGE.)

Adults (12 years of age and older): Approximately one-half of the ointment from the single-use tube should be applied into one nostril and the other half into the other nostril twice daily (morning and evening) for 5 days.

After application, the nostrils should be closed by pressing together and releasing the sides of the nose repetitively for approximately 1 minute. This will spread the ointment throughout the nares.

The single-use 1.0 gram tube will deliver a total of approximately 0.5 gram of the ointment (approximately 0.25 gram/nostril).

The tube should be discarded after usage; it should not be re-used.

The safety and effectiveness of applications of this medication for greater than 5 days have not been established. There are no human clinical or pre-clinical animal data to support the use of this product in a chronic manner or in manners other than those described in this package insert.

Until further information is known, *Bactroban* Nasal should not be applied concurrently with any other intranasal products.

HOW SUPPLIED

Bactroban Nasal (mupirocin calcium ointment), 2% is supplied in 1.0 gram tubes packaged in cartons of 10.

NDC 0029-1526-11 (1.0 gram tubes in packages of 10). Store at or below 25°C (77°F).

REFERENCE

1. National Committee for Clinical Laboratory Standards. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically—Third Edition; Approved Standard NCCLS Document M7-A3. Vol. 12, No. 25, NCCLS, Villanova, PA, December 1993.

Manufactured by **DPT Laboratories, Inc.**
San Antonio, TX 78215
Distributed by **SmithKline Beecham Pharmaceuticals**
Philadelphia, PA 19101
BN:L1

COMPAZINE® ℞

[*komp'ah-zeen*]
(brand of prochlorperazine)

DESCRIPTION

Tablets—Each round, yellow-green, coated tablet contains prochlorperazine maleate equivalent to prochlorperazine as follows: 5 mg imprinted SKF and C66; 10 mg imprinted SKF and C67.

5 mg and 10 mg Tablets: Modified Formulation—Inactive ingredients consist of cellulose, lactose, magnesium stearate, polyethylene glycol, sodium croscarmellose, titanium dioxide, D&C Yellow No. 10, FD&C Blue No. 2, FD&C Yellow No. 6, FD&C Red No. 40, iron oxide, starch, stearic acid and trace amounts of other inactive ingredients.

NOTE: *Compazine* 5 mg and 10 mg tablets have been changed from yellow-green sugar-coated tablets to yellow-green film-coated tablets. The film-coated tablets are smaller in size than the sugar-coated tablets. The inactive ingredients have changed, but the drug content remains unchanged.

Spansule® sustained release capsules—Each Compazine® *Spansule* capsule is so prepared that an initial dose is released promptly and the remaining medication is released gradually over a prolonged period.

Each capsule, with black cap and natural body, contains prochlorperazine maleate equivalent to prochlorperazine as follows: 10 mg imprinted SKF and C44; 15 mg imprinted SKF and C46. Inactive ingredients consist of benzyl alcohol, cetylpyridinium chloride, D&C Green No. 5, D&C Yellow No. 10, FD&C Blue No. 1, FD&C Red No. 40, FD&C Yellow No. 6, gelatin, glyceryl monostearate, sodium lauryl sulfate, starch, sucrose, wax and trace amounts of other inactive ingredients.

Vials, 2 mL (5 mg/mL) and 10 mL (5 mg/mL)—Each mL contains, in aqueous solution, 5 mg prochlorperazine as the edisylate, 5 mg sodium biphosphate, 12 mg sodium tartrate, 0.9 mg sodium saccharin and 0.75% benzyl alcohol as preservative.

Disposable Syringes, 2 mL (5 mg/mL)—Each mL contains, in aqueous solution, 5 mg prochlorperazine as the edisylate, 5 mg sodium biphosphate, 12 mg sodium tartrate, 0.9 mg sodium saccharin and 0.75% benzyl alcohol as preservative.

Suppositories—Each suppository contains $2^1/_2$ mg, 5 mg or 25 mg of prochlorperazine; with glycerin, glyceryl monopalmitate, glyceryl monostearate, hydrogenated cocoanut oil fatty acids and hydrogenated palm kernel oil fatty acids.

Syrup—Each 5 mL (1 teaspoonful) of clear, yellow-orange, fruit-flavored liquid contains 5 mg of prochlorperazine as the edisylate. Inactive ingredients consist of FD&C Yellow No. 6, flavors, polyoxyethylene polyoxypropylene glycol, sodium benzoate, sodium citrate, sucrose and water.

INDICATIONS

For control of severe nausea and vomiting.

For management of the manifestations of psychotic disorders.

Compazine (prochlorperazine) is effective for the short-term treatment of generalized non-psychotic anxiety. However, *Compazine* is not the first drug to be used in therapy for most patients with non-psychotic anxiety, because certain risks associated with its use are not shared by common alternative treatments (e.g., benzodiazepines).

When used in the treatment of non-psychotic anxiety, *Compazine* should not be administered at doses of more than 20 mg per day or for longer than 12 weeks, because the use of *Compazine* at higher doses or for longer intervals may cause persistent tardive dyskinesia that may prove irreversible (see Warnings).

The effectiveness of *Compazine* as treatment for non-psychotic anxiety was established in 4-week clinical studies of outpatients with generalized anxiety disorder. This evidence does not predict that *Compazine* will be useful in patients with other non-psychotic conditions in which anxiety, or signs that mimic anxiety, are found (e.g., physical illness, organic mental conditions, agitated depression, character pathologies, etc.).

Compazine has not been shown effective in the management of behavioral complications in patients with mental retardation.

CONTRAINDICATIONS

Do not use in patients with known hypersensitivity to phenothiazines.

Do not use in comatose states or in the presence of large amounts of central nervous system depressants (alcohol, barbiturates, narcotics, etc.).

Do not use in pediatric surgery.

Do not use in children under 2 years of age or under 20 lbs.

Do not use in children for conditions for which dosage has not been established.

WARNINGS

The extrapyramidal symptoms which can occur secondary to Compazine (prochlorperazine) may be confused with the central nervous system signs of an undiagnosed primary disease responsible for the vomiting, e.g., Reye's syndrome or other encephalopathy. The use of Compazine (prochlorperazine) and other potential hepatotoxins should be avoided in children and adolescents whose signs and symptoms suggest Reye's syndrome.

Tardive Dyskinesia: Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, may develop in patients treated with neuroleptic (antipsychotic) drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of neuroleptic treatment, which patients are likely to develop the syndrome. Whether neuroleptic drug products differ in their potential to cause tardive dyskinesia is unknown.

Both the risk of developing the syndrome and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of neuroleptic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses.

There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if neuroleptic treatment is withdrawn. Neuroleptic treatment itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying disease process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown.

Given these considerations, neuroleptics should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic neuroleptic treatment should generally be reserved for patients who suffer from a chronic illness that, 1) is known to respond to neuroleptic drugs, and 2) for whom alternative, equally effective, but potentially less harmful treatments are *not* available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically.

If signs and symptoms of tardive dyskinesia appear in a patient on neuroleptics, drug discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome.

For further information about the description of tardive dyskinesia and its clinical detection, please refer to the sections on PRECAUTIONS and ADVERSE REACTIONS.

Neuroleptic Malignant Syndrome (NMS): A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental sta-

evidence of autonomic instability (irregular pulse
blood pressure, tachycardia, diaphoresis and cardiac
dysrhythmias).
diagnostic evaluation of patients with this syndrome is
indicated. In arriving at a diagnosis, it is important to
identify cases where the clinical presentation includes both
some medical illness (e.g., pneumonia, systemic infection,
etc.) and untreated or inadequately treated extrapyramidal
signs and symptoms (EPS). Other important considerations
in the differential diagnosis include central anticholinergic
toxicity, heat stroke, drug fever and primary central nervous
system (CNS) pathology.
The management of NMS should include 1) immediate dis-
continuation of antipsychotic drugs and other drugs not es-
sential to concurrent therapy, 2) intensive symptomatic
treatment and medical monitoring, and 3) treatment of any
concomitant serious medical problems for which specific
treatments are available. There is no general agreement
about specific pharmacological treatment regimens for
uncomplicated NMS.
If a patient requires antipsychotic drug treatment after re-
covery from NMS, the potential reintroduction of drug ther-
apy should be carefully considered. The patient should be
carefully monitored, since recurrences of NMS have been
reported.
An encephalopathic syndrome (characterized by weakness,
lethargy, fever, tremulousness and confusion, extrapyrami-
dal symptoms, leukocytosis, elevated serum enzymes, BUN
and FBS) has occurred in a few patients treated with lithium
plus a neuroleptic. In some instances, the syndrome was fol-
lowed by irreversible brain damage. Because of a possible
causal relationship between these events and the concomi-
tant administration of lithium and neuroleptics, patients
receiving such combined therapy should be monitored
closely for early evidence of neurologic toxicity and treat-
ment discontinued promptly if such signs appear. This en-
cephalopathic syndrome may be similar to or the same as
neuroleptic malignant syndrome (NMS).
Patients with bone marrow depression or who have previ-
ously demonstrated a hypersensitivity reaction (e.g., blood
dyscrasias, jaundice) with a phenothiazine should not re-
ceive any phenothiazine, including *Compazine*, unless in the
judgment of the physician the potential benefits of treat-
ment outweigh the possible hazards.
Compazine (prochlorperazine) may impair mental and/or
physical abilities, especially during the first few days of ther-
apy. Therefore, caution patients about activities requiring
alertness (e.g., operating vehicles or machinery).
Phenothiazines may intensify or prolong the action of cen-
tral nervous system depressants (e.g., alcohol, anesthetics,
narcotics).
Use in Pregnancy: Safety for the use of *Compazine*
during pregnancy has not been established. Therefore,
Compazine is not recommended for use in pregnant patients
except in cases of severe nausea and vomiting that are so
severe and intractable that, in the judgment of the physi-
cian, drug intervention is required and potential benefits
outweigh possible hazards.
There have been reported instances of prolonged jaundice,
extrapyramidal signs, hyperreflexia or hyporeflexia in new-
born infants whose mothers received phenothiazines.
Nursing Mothers: There is evidence that phenothiazines
are excreted in the breast milk of nursing mothers. Caution
should be exercised when *Compazine* is administered to a
nursing woman.

PRECAUTIONS

The antiemetic action of Compazine (prochlorperazine) may
mask the signs and symptoms of overdosage of other drugs
or may obscure the diagnosis and treatment of other condi-
tions such as intestinal obstruction, brain tumor and Reye's
syndrome (see Warnings).
When *Compazine* is used with cancer chemotherapeutic
agents, vomiting as a sign of the toxicity of these agents may
be obscured by the antiemetic effect of *Compazine*.
Because hypotension may occur, large doses and parenteral
administration should be used cautiously in patients with
impaired cardiovascular systems. To minimize the occur-
rence of hypotension after injection, keep patient lying down
and observe for at least $^1/_2$ hour. If hypotension occurs after
parenteral or oral dosing, place patient in head-low position
with legs raised. If a vasoconstrictor is required, Levo-
phed® and Neo-Synephrine®† are suitable. Other pressor
agents, including epinephrine, should not be used because
they may cause a paradoxical further lowering of blood
pressure.
Aspiration of vomitus has occurred in a few post-surgical
patients who have received Compazine (prochlorperazine) as
an antiemetic. Although no causal relationship has been
established, this possibility should be borne in mind during
postoperative aftercare.
Coma, deep sleep, from which patients can be aroused, and coma
have been reported, usually with overdosage.
Neuroleptic drugs elevate prolactin levels; the elevation
persists during chronic administration. Tissue culture exper-
iments indicate that approximately one third of human
breast cancers are prolactin-dependent *in vitro*, a factor of
potential importance if the prescribing of these drugs is con-
templated in a patient with a previously detected breast can-
cer. Although disturbances such as galactorrhea, amenor-
rhea, gynecomastia and impotence have been reported, the
clinical significance of elevated serum prolactin levels is
unknown for most patients. An increase in mammary neo-
plasms has been found in rodents after chronic administra-
tion of neuroleptic drugs. Neither clinical nor epidemiologic
studies conducted to date, however, have shown an associa-
tion between chronic administration of these drugs and
mammary tumorigenesis; the available evidence is consid-
ered too limited to be conclusive at this time.
Chromosomal aberrations in spermatocytes and abnormal
sperm have been demonstrated in rodents treated with
certain neuroleptics.
As with all drugs which exert an anticholinergic effect,
and/or cause mydriasis, prochlorperazine should be used
with caution in patients with glaucoma.
Because phenothiazines may interfere with thermoregulatory
mechanisms, use with caution in persons who will be
exposed to extreme heat.
Phenothiazines can diminish the effect of oral anticoagu-
lants.
Phenothiazines can produce alpha-adrenergic blockade.
Thiazide diuretics may accentuate the orthostatic hypoten-
sion that may occur with phenothiazines.
Antihypertensive effects of guanethidine and related com-
pounds may be counteracted when phenothiazines are used
concomitantly.
Concomitant administration of propranolol with phenothia-
zines results in increased plasma levels of both drugs.
Phenothiazines may lower the convulsive threshold; dosage
adjustments of anticonvulsants may be necessary. Potentia-
tion of anticonvulsant effects does not occur. However, it has
been reported that phenothiazines may interfere with the
metabolism of Dilantin®‡ and thus precipitate *Dilantin*
toxicity.
The presence of phenothiazines may produce false-positive
phenylketonuria (PKU) test results.
Long-Term Therapy: Given the likelihood that some pa-
tients exposed chronically to neuroleptics will develop tar-
dive dyskinesia, it is advised that all patients in whom
chronic use is contemplated be given, if possible, full infor-
mation about this risk. The decision to inform patients and/
or their guardians must obviously take into account the clini-
cal circumstances and the competency of the patient to
understand the information provided.
To lessen the likelihood of adverse reactions related to cumu-
lative drug effect, patients with a history of long-term ther-
apy with Compazine (prochlorperazine) and/or other neuro-
leptics should be evaluated periodically to decide whether
the maintenance dosage could be lowered or drug therapy
discontinued.
**Children with acute illnesses (e.g., chickenpox, CNS infec-
tions, measles, gastroenteritis) or dehydration seem to be
much more susceptible to neuromuscular reactions, particu-
larly dystonias, than are adults. In such patients, the drug
should be used only under close supervision.**
Drugs which lower the seizure threshold, including pheno-
thiazine derivatives, should not be used with Amipaque®§.
As with other phenothiazine derivatives, Compazine (pro-
chlorperazine) should be discontinued at least 48 hours be-
fore myelography, should not be resumed for at least 24
hours postprocedure, and should not be used for the control
of nausea and vomiting occurring either prior to myelogra-
phy with *Amipaque*, or postprocedure.

ADVERSE REACTIONS

Drowsiness, dizziness, amenorrhea, blurred vision, skin
reactions and hypotension may occur. Neuroleptic Malig-
nant Syndrome (NMS) has been reported in association with
antipsychotic drugs (see WARNINGS).
Cholestatic jaundice has occurred. If fever with grippe-like
symptoms occurs, appropriate liver studies should be con-
ducted. If tests indicate an abnormality, stop treatment.
There have been a few observations of fatty changes in the
livers of patients who have died while receiving the drug. No
causal relationship has been established.
Leukopenia and agranulocytosis have occurred. Warn pa-
tients to report the sudden appearance of sore throat or other
signs of infection. If white blood cell and differential counts
indicate leukocyte depression, stop treatment and start
antibiotic and other suitable therapy.
Neuromuscular (Extrapyramidal) Reactions
These symptoms are seen in a significant number of hospital-
ized mental patients. They may be characterized by motor
restlessness, be of the dystonic type, or they may resemble
parkinsonism.
Depending on the severity of symptoms, dosage should be
reduced or discontinued. If therapy is reinstituted, it should
be at a lower dosage. Should these symptoms occur in chil-
dren or pregnant patients, the drug should be stopped and
not reinstituted. In most cases barbiturates by suitable route
of administration will suffice. (Or, injectable Benadryl®‖
may be useful.) In more severe cases, the administration of
an anti-parkinsonism agent, except levodopa, usually pro-
duces rapid reversal of symptoms. Suitable supportive mea-
sures such as maintaining a clear airway and adequate
hydration should be employed.
Motor Restlessness: Symptoms may include agitation or
jitteriness and sometimes insomnia. These symptoms often
disappear spontaneously. At times these symptoms may be
similar to the original neurotic or psychotic symptoms. Dos-
age should not be increased until these side effects have
subsided.
If these symptoms become too troublesome, they can usually
be controlled by a reduction of dosage or change of drug.
Treatment with anti-parkinsonian agents, benzodiazepines
or propranolol may be helpful.
Dystonias: Symptoms may include: spasm of the neck mus-
cles, sometimes progressing to torticollis; extensor rigidity of
back muscles, sometimes progressing to opisthotonos; carpo-
pedal spasm, trismus, swallowing difficulty, oculogyric crisis
and protrusion of the tongue.
These usually subside within a few hours, and almost always
within 24 to 48 hours, after the drug has been discontinued.
In mild cases, reassurance or a barbiturate is often sufficient.
In moderate cases, barbiturates will usually bring rapid re-
lief. *In more severe adult cases,* the administration of an anti-
parkinsonism agent, except levodopa, usually produces rapid
reversal of symptoms. *In children,* reassurance and barbitu-
rates will usually control symptoms. (Or, injectable *Benadryl*
may be useful. Note: See *Benadryl* prescribing information
for appropriate *children's* dosage.) If appropriate treatment
with anti-parkinsonism agents or *Benadryl* fails to reverse
the signs and symptoms, the diagnosis should be reevalu-
ated.
Pseudo-parkinsonism: Symptoms may include: mask-like
facies; drooling; tremors; pillrolling motion; cogwheel rigid-
ity; and shuffling gait. Reassurance and sedation are impor-
tant. In most cases these symptoms are readily controlled
when an anti-parkinsonism agent is administered concomi-
tantly. Anti-parkinsonism agents should be used only when
required. Generally, therapy of a few weeks to 2 or 3 months
will suffice. After this time patients should be evaluated to
determine their need for continued treatment. (Note:
Levodopa has not been found effective in pseudo-parkinson-
ism.) Occasionally it is necessary to lower the dosage of
Compazine (prochlorperazine) or to discontinue the drug.
Tardive Dyskinesia: As with all antipsychotic agents, tar-
dive dyskinesia may appear in some patients on long-term
therapy or may appear after drug therapy has been discon-
tinued. The syndrome can also develop, although much less
frequently, after relatively brief treatment periods at low
doses. This syndrome appears in all age groups. Although its
prevalence appears to be highest among elderly patients,
especially elderly women, it is impossible to rely upon preva-
lence estimates to predict at the inception of neuroleptic
treatment which patients are likely to develop the syn-
drome. The symptoms are persistent and in some patients
appear to be irreversible. The syndrome is characterized by
rhythmical involuntary movements of the tongue, face,
mouth or jaw (e.g., protrusion of tongue, puffing of cheeks,
puckering of mouth, chewing movements). Sometimes these
may be accompanied by involuntary movements of extremi-
ties. In rare instances, these involuntary movements of the
extremities are the only manifestations of tardive dyskine-
sia. A variant of tardive dyskinesia, tardive dystonia, has
also been described.
There is no known effective treatment for tardive dyskine-
sia; anti-parkinsonism agents do not alleviate the symptoms
of this syndrome. It is suggested that all antipsychotic agents
be discontinued if these symptoms appear.
Should it be necessary to reinstitute treatment, or increase
the dosage of the agent, or switch to a different antipsychotic
agent, the syndrome may be masked.
It has been reported that fine vermicular movements of the
tongue may be an early sign of the syndrome and if the medi-
cation is stopped at that time the syndrome may not develop.
Contact Dermatitis: Avoid getting the Injection solution
on hands or clothing because of the possibility of contact
dermatitis.
**Adverse Reactions Reported with Compazine (prochlorpera-
zine) or Other Phenothiazine Derivatives:** Adverse reactions
with different phenothiazines vary in type, frequency and
mechanism of occurrence, i.e., some are dose-related, while
others involve individual patient sensitivity. Some adverse
reactions may be more likely to occur, or occur with greater
intensity, in patients with special medical problems, e.g.,
patients with mitral insufficiency or pheochromocytoma

Continued on next page

SmithKline Beecham—Cont.

have experienced severe hypotension following recommended doses of certain phenothiazines.

Not all of the following adverse reactions have been observed with every phenothiazine derivative, but they have been reported with 1 or more and should be borne in mind when drugs of this class are administered: extrapyramidal symptoms (opisthotonos, oculogyric crisis, hyperreflexia, dystonia, akathisia, dyskinesia, parkinsonism) some of which have lasted months and even years—particularly in elderly patients with previous brain damage; grand mal and petit mal convulsions, particularly in patients with EEG abnormalities or history of such disorders; altered cerebrospinal fluid proteins; cerebral edema; intensification and prolongation of the action of central nervous system depressants (opiates, analgesics, antihistamines, barbiturates, alcohol), atropine, heat, organophosphorus insecticides; autonomic reactions (dryness of mouth, nasal congestion, headache, nausea, constipation, obstipation, adynamic ileus, ejaculatory disorders/impotence, priapism, atonic colon, urinary retention, miosis and mydriasis); reactivation of psychotic processes, catatonic-like states; hypotension (sometimes fatal); cardiac arrest; blood dyscrasias (pancytopenia, thrombocytopenic purpura, leukopenia, agranulocytosis, eosinophilia, hemolytic anemia, aplastic anemia); liver damage (jaundice, biliary stasis); endocrine disturbances (hyperglycemia, hypoglycemia, glycosuria, lactation, galactorrhea, gynecomastia, menstrual irregularities, false-positive pregnancy tests); skin disorders (photosensitivity, itching, erythema, urticaria, eczema up to exfoliative dermatitis); other allergic reactions (asthma, laryngeal edema, angioneurotic edema, anaphylactoid reactions); peripheral edema; reversed epinephrine effect; hyperpyrexia; mild fever after large I.M. doses; increased appetite; increased weight; a systemic lupus erythematosus-like syndrome; pigmentary retinopathy; with prolonged administration of substantial doses, skin pigmentation, epithelial keratopathy, and lenticular and corneal deposits.

EKG changes—particularly nonspecific, usually reversible Q and T wave distortions—have been observed in some patients receiving phenothiazine tranquilizers.

Although phenothiazines cause neither psychic nor physical dependence, sudden discontinuance in long-term psychiatric patients may cause temporary symptoms, e.g., nausea and vomiting, dizziness, tremulousness.

Note: There have been occasional reports of sudden death in patients receiving phenothiazines. In some cases, the cause appeared to be cardiac arrest or asphyxia due to failure of the cough reflex.

DOSAGE AND ADMINISTRATION

Notes on Injection: *Stability*—This solution should be protected from light. This is a clear, colorless to pale yellow solution; a slight yellowish discoloration will not alter potency. If markedly discolored, solution should be discarded.

Compatibility—It is recommended that Compazine (prochlorperazine) Injection not be mixed with other agents in the syringe.

DOSAGE AND ADMINISTRATION—ADULTS

(For children's dosage and administration, see below.) Dosage should be increased more gradually in debilitated or emaciated patients.

Elderly Patients: In general, dosages in the lower range are sufficient for most elderly patients. Since they appear to be more susceptible to hypotension and neuromuscular reactions, such patients should be observed closely. Dosage should be tailored to the individual, response carefully monitored and dosage adjusted accordingly. Dosage should be increased more gradually in elderly patients.

1. To Control Severe Nausea and Vomiting: Adjust dosage to the response of the individual. Begin with the lowest recommended dosage.

Oral Dosage—Tablets: Usually one 5 mg or 10 mg tablet 3 or 4 times daily. Daily dosages above 40 mg should be used only in resistant cases.

***Spansule* capsules:** Initially, usually one 15 mg capsule on arising or one 10 mg capsule q12h. Daily doses above 40 mg should be used only in resistant cases.

Rectal Dosage: 25 mg twice daily.

I.M. Dosage: Initially 5 to 10 mg (1 to 2 mL) injected *deeply* into the upper outer quadrant of the buttock. If necessary, repeat every 3 or 4 hours. Total I.M. dosage should not exceed 40 mg per day.

I.V. Dosage: $2^1/_2$ to 10 mg ($^1/_2$ to 2 mL) by slow I.V. injection or infusion at a rate not to exceed 5 mg per minute. *Compazine* Injection may be administered either undiluted or diluted in isotonic solution. A single dose of the drug should not exceed 10 mg; total I.V. dosage should not exceed 40 mg per day. When administered I.V., do not use bolus injection. Hypotension is a possibility if the drug is given by I.V. injection or infusion.

Subcutaneous administration is not advisable because of local irritation.

2. Adult Surgery (for severe nausea and vomiting): Total parenteral dosage should not exceed 40 mg per day. Hypotension is a possibility if the drug is given by I.V. injection or infusion.

I.M. Dosage: 5 to 10 mg (1 to 2 mL) 1 to 2 hours before induction of anesthesia (repeat once in 30 minutes, if necessary), or to control acute symptoms during and after surgery (repeat once if necessary).

I.V. Dosage: 5 to 10 mg (1 to 2 mL) as a slow I.V. injection or infusion 15 to 30 minutes before induction of anesthesia, or to control acute symptoms during or after surgery. Repeat once if necessary. Compazine (prochlorperazine) may be administered either undiluted or diluted in isotonic solution, but a single dose of the drug should not exceed 10 mg. The rate of administration should not exceed 5 mg per minute. When administered I.V., do not use bolus injection.

3. In Adult Psychiatric Disorders: Adjust dosage to the response of the individual and according to the severity of the condition. Begin with the lowest recommended dose. Although response ordinarily is seen within a day or 2, longer treatment is usually required before maximal improvement is seen.

Oral Dosage: *Non-Psychotic Anxiety*—Usual dosage is 5 mg 3 or 4 times daily; by *Spansule* capsule, usually one 15 mg capsule on arising or one 10 mg capsule q12h. Do not administer in doses of more than 20 mg per day or for longer than 12 weeks.

Psychotic Disorders—In relatively mild conditions, as seen in private psychiatric practice or in outpatient clinics, dosage is 5 or 10 mg 3 or 4 times daily.

In moderate to severe conditions, for hospitalized or adequately supervised patients, usual starting dosage is 10 mg 3 or 4 times daily. Increase dosage gradually until symptoms are controlled or side effects become bothersome. When dosage is increased by small increments every 2 or 3 days, side effects either do not occur or are easily controlled. Some patients respond satisfactorily on 50 to 75 mg daily.

In more severe disturbances, optimum dosage is usually 100 to 150 mg daily.

I.M. Dosage: For immediate control of severely disturbed adults, inject an initial dose of 10 to 20 mg (2 to 4 mL) *deeply* into the upper outer quadrant of the buttock. Many patients respond shortly after the first injection. If necessary, however, repeat the initial dose every 2 to 4 hours (or, in resistant cases, every hour) to gain control of the patient. More than three or four doses are seldom necessary. After control is achieved, switch patient to an oral form of the drug at the same dosage level or higher. If, in rare cases, parenteral therapy is needed for a prolonged period, give 10 to 20 mg (2 to 4 mL) every 4 to 6 hours. Pain and irritation at the site of injection have seldom occurred.

Subcutaneous administration is not advisable because of local irritation.

DOSAGE AND ADMINISTRATION—CHILDREN

Do not use in pediatric surgery.

Children seem more prone to develop extrapyramidal reactions, even on moderate doses. Therefore, use lowest effective dosage. Tell parents not to exceed prescribed dosage, since the possibility of adverse reactions increases as dosage rises. Occasionally the patient may react to the drug with signs of restlessness and excitement; if this occurs, do not administer additional doses. Take particular precaution in administering the drug to children with acute illnesses or dehydration (see under Dystonias).

When writing a prescription for the $2^1/_2$ mg size suppository, write "$2^1/_2$," not "2.5"; this will help avoid confusion with the 25 mg adult size.

1. Severe Nausea and Vomiting in Children: Compazine (prochlorperazine) should not be used in children under 20 pounds in weight or 2 years of age. It should not be used in conditions for which children's dosages have not been established. Dosage and frequency of administration should be adjusted according to the severity of the symptoms and the response of the patient. The duration of activity following intramuscular administration may last up to 12 hours. Subsequent doses may be given by the same route if necessary.

Oral or Rectal Dosage: More than 1 day's therapy is seldom necessary.

Weight	Usual Dosage	Not to Exceed
under 20 lbs not recommended		
20 to 29 lbs	$2^1/_2$ mg 1 or 2 times a day	7.5 mg per day
30 to 39 lbs	$2^1/_2$ mg 2 or 3 times a day	10 mg per day
40 to 85 lbs	$2^1/_2$ mg 3 times a day or 5 mg 2 times a day	15 mg per day

I.M. Dosage: Calculate each dose on the basis of 0.06 mg of the drug per lb of body weight; give by deep I.M. injection. Control is usually obtained with one dose.

2. In Psychotic Children:

Oral or Rectal Dosage: For children 2 to 12 years, starting dosage is $2^1/_2$ mg 2 or 3 times daily. Do not give more than 10 mg the first day. Then increase dosage according to patient's response.

FOR AGES 2 to 5, total daily dosage usually does not exceed 20 mg.

FOR AGES 6 to 12, total daily dosage usually does not exceed 25 mg.

I.M. Dosage: For ages under 12, calculate each dose on the basis of 0.06 mg of Compazine (prochlorperazine) per lb of body weight; give by deep I.M. injection. Control is usually obtained with one dose. After control is achieved, switch the patient to an oral form of the drug at the same dosage level or higher.

OVERDOSAGE

(See also Adverse Reactions.)

SYMPTOMS—Primarily involvement of the extrapyramidal mechanism producing some of the dystonic reactions described above.

Symptoms of central nervous system depression to the point of somnolence or coma. Agitation and restlessness may also occur. Other possible manifestations include convulsions, EKG changes and cardiac arrhythmias, fever and autonomic reactions such as hypotension, dry mouth and ileus.

TREATMENT—It is important to determine other medications taken by the patient since multiple-dose therapy is common in overdosage situations. Treatment is essentially symptomatic and supportive. Early gastric lavage is helpful. Keep patient under observation and maintain an open airway, since involvement of the extrapyramidal mechanism may produce dysphagia and respiratory difficulty in severe overdosage. **Do not attempt to induce emesis because a dystonic reaction of the head or neck may develop that could result in aspiration of vomitus.** Extrapyramidal symptoms may be treated with anti-parkinsonism drugs, barbiturates or *Benadryl*. See prescribing information for these products. Care should be taken to avoid increasing respiratory depression.

If administration of a stimulant is desirable, amphetamine, dextroamphetamine or caffeine with sodium benzoate is recommended.

Stimulants that may cause convulsions (e.g., picrotoxin or pentylenetetrazol) should be avoided.

If hypotension occurs, the standard measures for managing circulatory shock should be initiated. If it is desirable to administer a vasoconstrictor, *Levophed* and *Neo-Synephrine* are most suitable. Other pressor agents, including epinephrine, are not recommended because phenothiazine derivatives may reverse the usual elevating action of these agents and cause a further lowering of blood pressure.

Limited experience indicates that phenothiazines are *not* dialyzable.

Special note on Spansule *capsules*—Since much of the *Spansule* capsule medication is coated for gradual release, therapy directed at reversing the effects of the ingested drug and at supporting the patient should be continued for as long as overdosage symptoms remain. Saline cathartics are useful for hastening evacuation of pellets that have not already released medication.

HOW SUPPLIED

Tablets—5 and 10 mg, in bottles of 100; in Single Unit Packages of 100 (intended for institutional use only).
5 mg 100's: NDC 0007-3366-20
5 mg SUP 100's: NDC 0007-3366-21
10 mg 100's: NDC 0007-3367-20
10 mg SUP 100's: NDC 0007-3367-21

***Spansule* capsules**—10 and 15 mg, in bottles of 50.
10 mg 50's: NDC 0007-3344-15
15 mg 50's: NDC 0007-3346-15

Vials—2 mL (5 mg/mL), in boxes of 25 and 10 mL (5 mg/mL), in boxes of 1.
2 mL (5 mg/mL), in boxes of 25: NDC 0007-3352-16
10 mL (5 mg/mL), in boxes of 1: NDC 0007-3343-01

Disposable Syringes—2 mL (5 mg/mL), in individual cartons.
2 mL (5 mg/mL), in boxes of 1: NDC 0007-3351-01

Suppositories—$2^1/_2$ mg (for young children), 5 mg (for older children) and 25 mg (for adults), in boxes of 12.
$2^1/_2$ mg, in boxes of 12: NDC 0007-3360-03
5 mg, in boxes of 12: NDC 0007-3361-03
25 mg, in boxes of 12: NDC 0007-3362-03

Syrup—5 mg/5 mL (1 teaspoonful) in 4 fl oz bottles.
5 mg/5 mL, 4 fl oz: NDC 0007-3363-44

Store Compazine (prochlorperazine) vials and syringes below 86°F. Do not freeze.

Veterans Administration/Military/PHS—Vials, 2 mL, 25's, 6505-01-230-3931; 10 mL, 1's, 6505-00-684-9630; Suppositories, $2^1/_2$ mg, 12's, 6505-00-133-5213; 5 mg, 12's, 6505-01-153-2894; 25 mg, 12's, 6505-00-133-5214; Syrup, 5 mg/5 mL, 4 fl oz, 6505-01-039-5849; Tablets, 5 mg, 100's, 6505-00-761-5640;

100's (SUP), 6505-00-118-2563; 10 mg, 100's, 6505-01-... 10 mg, 100's (SUP), 6505-00-092-3139.

...ephrine bitartrate, Sanofi Winthrop Pharmaceuti...

...ephrine hydrochloride, Sanofi Winthrop Pharma...

...in, Parke-Davis.
...mide, Sanofi Winthrop Pharmaceuticals.
...hydramine hydrochloride, Parke-Davis.

...Shown in Product Identification Guide, page 336

...OMEL® ℞
[...'mel]
...of liothyronine sodium

...RIPTION
...hormone drugs are natural or synthetic prepara... containing tetraiodothyronine (T_4, levothyroxine) so... or triiodothyronine (T_3, liothyronine) sodium or both. ... T_3 are produced in the human thyroid gland by the ...ation and coupling of the amino acid tyrosine. T_4 con... four iodine atoms and is formed by the coupling of two ...ules of diiodotyrosine (DIT). T_3 contains three atoms of ... and is formed by the coupling of one molecule of DIT ... one molecule of monoiodotyrosine (MIT). Both hor... are stored in the thyroid colloid as thyroglobulin.
...hormone preparations belong to two categories: (1) ...al hormonal preparations derived from animal thy... and (2) synthetic preparations. Natural preparations ...de desiccated thyroid and thyroglobulin. Desiccated ...d is derived from domesticated animals that are used ...od by man (either beef or hog thyroid), and thyroglobu... derived from thyroid glands of the hog. The United ...Pharmacopeia (USP) has standardized the total iodine ...nt of natural preparations. Thyroid USP contains not ...than (NLT) 0.17 percent and not more than (NMT) 0.23 ...ent iodine, and thyroglobulin contains not less than ...0.7 percent of organically bound iodine. Iodine con... is only an indirect indicator of true hormonal biologic ...ity.
...mel (liothyronine sodium) Tablets contain liothyronine ...iiodothyronine or LT_3), a synthetic form of a natural ...d hormone, and is available as the sodium salt.
...ty-five mcg of liothyronine is equivalent to approxi... 1 grain of desiccated thyroid or thyroglobulin and 0.1 ... L-thyroxine.
...round, white to off-white Cytomel (liothyronine so... tablet contains liothyronine sodium equivalent to lio...nine as follows: 5 mcg debossed SKF and D14; 25 mcg ...d and debossed SKF and D16; 50 mcg scored and ...ed SKF and D17. Inactive ingredients consist of cal... sulfate, gelatin, starch, stearic acid, sucrose and talc.

...ICAL PHARMACOLOGY
...mechanisms by which thyroid hormones exert their ...logic action are not well understood. These hormones ...ce oxygen consumption by most tissues of the body, ...se the basal metabolic rate and the metabolism of car...drates, lipids and proteins. Thus, they exert a profound ...ence on every organ system in the body and are of par...lar importance in the development of the central ner... system.

...macokinetics
...e liothyronine sodium (T_3) is not firmly bound to serum ...in, it is readily available to body tissues. The onset of ...ity of liothyronine sodium is rapid, occurring within a ...hours. Maximum pharmacologic response occurs within ... days, providing early clinical response. The biological ...life is about 2-1/2 days.
... almost totally absorbed, 95 percent in 4 hours. The hor... contained in the natural preparations are absorbed in ...nner similar to the synthetic hormones.
...yronine sodium has a rapid cutoff of activity which ...s quick dosage adjustment and facilitates control of ...effects of overdosage, should they occur.
...higher affinity of levothyroxine (T_4) for both thyroid-...ng globulin and thyroid-binding prealbumin as com...d to triiodothyronine (T_3) partially explains the higher ... levels and longer half-life of the former hormone. ...protein-bound hormones exist in reverse equilibrium ... minute amounts of free hormone, the latter accounting ... the metabolic activity.

...CATIONS AND USAGE
...d hormone drugs are indicated:
...replacement or supplemental therapy in patients with ...hypothyroidism of any etiology, except transient hypothy...ism during the recovery phase of subacute thyroiditis. ...category includes cretinism, myxedema and ordinary ...hypothyroidism in patients of any age (pediatric patients, ..., the elderly), or state (including pregnancy); primary hypothyroidism resulting from functional deficiency, primary atrophy, partial or total absence of thyroid gland, or the effects of surgery, radiation, or drugs, with or without the presence of goiter; and secondary (pituitary) or tertiary (hypothalamic) hypothyroidism (See WARNINGS).
2. As pituitary thyroid-stimulating hormone (TSH) suppressants, in the treatment or prevention of various types of euthyroid goiters, including thyroid nodules, subacute or chronic lymphocytic thyroiditis (Hashimoto's) and multinodular goiter.
3. As diagnostic agents in suppression tests to differentiate suspected mild hyperthyroidism or thyroid gland autonomy.

Cytomel (liothyronine sodium) Tablets can be used in patients allergic to desiccated thyroid or thyroid extract derived from pork or beef.

CONTRAINDICATIONS

Thyroid hormone preparations are generally contraindicated in patients with diagnosed but as yet uncorrected adrenal cortical insufficiency, untreated thyrotoxicosis and apparent hypersensitivity to any of their active or extraneous constituents. There is no well-documented evidence from the literature, however, of true allergic or idiosyncratic reactions to thyroid hormone.

WARNINGS

> Drugs with thyroid hormone activity, alone or together with other therapeutic agents, have been used for the treatment of obesity. In euthyroid patients, doses within the range of daily hormonal requirements are ineffective for weight reduction. Larger doses may produce serious or even life-threatening manifestations of toxicity, particularly when given in association with sympathomimetic amines such as those used for their anorectic effects.

The use of thyroid hormones in the therapy of obesity, alone or combined with other drugs, is unjustified and has been shown to be ineffective. Neither is their use justified for the treatment of male or female infertility unless this condition is accompanied by hypothyroidism.

Thyroid hormones should be used with great caution in a number of circumstances where the integrity of the cardiovascular system, particularly the coronary arteries, is suspected. These include patients with angina pectoris or the elderly, in whom there is a greater likelihood of occult cardiac disease. In these patients, liothyronine sodium therapy should be initiated with low doses, with due consideration for its relatively rapid onset of action. Starting dosage of Cytomel (liothyronine sodium) Tablets is 5 mcg daily, and should be increased by no more than 5 mcg increments at 2-week intervals. When, in such patients, a euthyroid state can only be reached at the expense of an aggravation of the cardiovascular disease, thyroid hormone dosage should be reduced.

Morphologic hypogonadism and nephrosis should be ruled out before the drug is administered. If hypopituitarism is present, the adrenal deficiency must be corrected prior to starting the drug.

Myxedematous patients are very sensitive to thyroid; dosage should be started at a very low level and increased gradually.

Severe and prolonged hypothyroidism can lead to a decreased level of adrenocortical activity commensurate with the lowered metabolic state. When thyroid-replacement therapy is administered, the metabolism increases at a greater rate than adrenocortical activity. This can precipitate adrenocortical insufficiency. Therefore, in severe and prolonged hypothyroidism, supplemental adrenocortical steroids may be necessary.

In rare instances the administration of thyroid hormone may precipitate a hyperthyroid state or may aggravate existing hyperthyroidism.

PRECAUTIONS

General—Thyroid hormone therapy in patients with concomitant diabetes mellitus or insipidus or adrenal cortical insufficiency aggravates the intensity of their symptoms. Appropriate adjustments of the various therapeutic measures directed at these concomitant endocrine diseases are required.

The therapy of myxedema coma requires simultaneous administration of glucocorticoids.

Hypothyroidism decreases and hyperthyroidism increases the sensitivity to oral anticoagulants. Prothrombin time should be closely monitored in thyroid-treated patients on oral anticoagulants and dosage of the latter agents adjusted on the basis of frequent prothrombin time determinations.

In infants, excessive doses of thyroid hormone preparations may produce craniosynostosis.

Information for the Patient—Patients on thyroid hormone preparations and parents of pediatric patients on thyroid therapy should be informed that:

1. Replacement therapy is to be taken essentially for life, with the exception of cases of transient hypothyroidism, usually associated with thyroiditis, and in those patients receiving a therapeutic trial of the drug.
2. They should immediately report during the course of therapy any signs or symptoms of thyroid hormone toxicity, e.g., chest pain, increased pulse rate, palpitations, excessive sweating, heat intolerance, nervousness, or any other unusual event.
3. In case of concomitant diabetes mellitus, the daily dosage of antidiabetic medication may need readjustment as thyroid hormone replacement is achieved. If thyroid medication is stopped, a downward readjustment of the dosage of insulin or oral hypoglycemic agent may be necessary to avoid hypoglycemia. At all times, close monitoring of urinary glucose levels is mandatory in such patients.
4. In case of concomitant oral anticoagulant therapy, the prothrombin time should be measured frequently to determine if the dosage of oral anticoagulants is to be readjusted.
5. Partial loss of hair may be experienced by pediatric patients in the first few months of thyroid therapy, but this is usually a transient phenomenon and later recovery is usually the rule.

Laboratory Tests—Treatment of patients with thyroid hormones requires the periodic assessment of thyroid status by means of appropriate laboratory tests besides the full clinical evaluation. The TSH suppression test can be used to test the effectiveness of any thyroid preparation, bearing in mind the relative insensitivity of the infant pituitary to the negative feedback effect of thyroid hormones. Serum T_4 levels can be used to test the effectiveness of all thyroid medications except products containing liothyronine sodium. When the total serum T_4 is low but TSH is normal, a test specific to assess unbound (free) T_4 levels is warranted. Specific measurements of T_4 and T_3 by competitive protein binding or radioimmunoassay are not influenced by blood levels of organic or inorganic iodine and have essentially replaced older tests of thyroid hormone measurements, i.e., PBI, BEI and T_4 by column.

Drug Interactions

Oral Anticoagulants—Thyroid hormones appear to increase catabolism of vitamin K-dependent clotting factors. If oral anticoagulants are also being given, compensatory increases in clotting factor synthesis are impaired. Patients stabilized on oral anticoagulants who are found to require thyroid replacement therapy should be watched very closely when thyroid is started. If a patient is truly hypothyroid, it is likely that a reduction in anticoagulant dosage will be required. No special precautions appear to be necessary when oral anticoagulant therapy is begun in a patient already stabilized on maintenance thyroid replacement therapy.

Insulin or Oral Hypoglycemics—Initiating thyroid replacement therapy may cause increases in insulin or oral hypoglycemic requirements. The effects seen are poorly understood and depend upon a variety of factors such as dose and type of thyroid preparations and endocrine status of the patient. Patients receiving insulin or oral hypoglycemics should be closely watched during initiation of thyroid replacement therapy.

Cholestyramine—Cholestyramine binds both T_4 and T_3 in the intestine, thus impairing absorption of these thyroid hormones. *In vitro* studies indicate that the binding is not easily removed. Therefore, 4 to 5 hours should elapse between administration of cholestyramine and thyroid hormones.

Estrogen, Oral Contraceptives—Estrogens tend to increase serum thyroxine-binding globulin (TBg). In a patient with a nonfunctioning thyroid gland who is receiving thyroid replacement therapy, free levothyroxine may be decreased when estrogens are started thus increasing thyroid requirements. However, if the patient's thyroid gland has sufficient function, the decreased free thyroxine will result in a compensatory increase in thyroxine output by the thyroid. Therefore, patients without a functioning thyroid gland who are on thyroid replacement therapy may need to increase their thyroid dose if estrogens or estrogen-containing oral contraceptives are given.

Tricyclic Antidepressants—Use of thyroid products with imipramine and other tricyclic antidepressants may increase receptor sensitivity and enhance antidepressant activity; transient cardiac arrhythmias have been observed. Thyroid hormone activity may also be enhanced.

Digitalis—Thyroid preparations may potentiate the toxic effects of digitalis. Thyroid hormonal replacement increases

Continued on next page

Information on the SmithKline Beecham Pharmaceuticals products appearing here is based on the labeling in effect on July 1, 1996. Further information on these and other products may be obtained from the Medical Department, SmithKline Beecham Pharmaceuticals, One Franklin Plaza, Philadelphia, PA 19101.